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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/051,727	01/17/2002	Rebanta Bandyopadhyay	LD0189 NP	8647

23914 7590 02/08/2005

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EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/051,727	BANDYOPADHYAY ET AL.	
	Examiner	Art Unit	
	Lakshmi S Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,10-13,15-17,19,22,30-32 and 34-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-6,8,10-13,30-32 and 34-54* is/are allowed.

6)☒ Claim(s) *15-17,19,22 and 56-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12-3-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of amendment, remarks and IDS all dated 12-3-04 is acknowledged.

Claims 1-6, 8, 10-13, 15-17, 19, 22, 30-32 and 34-58 are pending. Claims 56-58 are newly added.

Allowable Subject Matter

Claims 1-6, 8, 10-13, 30-32 and 34-54 are allowed, for the reasons explained in the previous action.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15, 16, 17, 19 and 22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-31 of U.S. Patent No. 6,689,802. Although the conflicting claims are not identical, they are not patentably distinct from each other. Instant claims recite a pharmaceutical preparation comprising a lyophilized epothilone analogue and a solvent for reconstituting epothilone analogue, wherein the solvent and the compound are separated in different vials. Dependent claims recite the carriers and amounts of epothilone. Patented claims are directed to pharmaceutical compositions comprising

a crystalline polymorph of an epothilone analogue together with carriers and diluents. Dependent claims of the patent are directed to methods of treating cancer or proliferative disorders comprising administering the composition containing Polymorphic crystalline form of epothilone analogue. Although instant claims differ from the patented claims in the form of the epothilone analogue i.e., lyophilized versus crystalline polymorph, the compositions in both sets of claims contain essentially the same compound dissolved in suitable solvents. Accordingly, once present in solution both sets of compositions do not exhibit substantial differences unless shown otherwise. Accordingly it would have been obvious for a skilled artisan at the time of the instant invention to prepare a composition of epothilone analogue comprising a crystalline or a lyophilized form, wherein the compound is dissolved in the solvent or separated until use and still achieve the same pharmacological effect.

Claims 15, 16, 17, 19, 22 and 56-58 are directed to an invention not patentably distinct from claims 1-31 of commonly assigned US Patent No. 6,689,802. Specifically, the patent discloses and claims exactly the same compound as that claimed in instant invention. Instant claims differ from the patented claims in the form of the epothilone analogue i.e., lyophilized versus crystalline polymorph; the compositions in both sets of claims contain essentially the same compound dissolved in suitable solvents. Accordingly, once present in solution both sets of compositions do not exhibit substantial differences unless shown otherwise. Accordingly it would have been obvious for a skilled artisan at the time of the instant invention to prepare a composition of epothilone analogue comprising a crystalline or a lyophilized form, wherein the compound is dissolved in the solvent or separated until use and still achieve the same pharmacological effect.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned US 6,689,802, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Claims 15, 16, 17, 19, 22 and 56-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,689,802 to DiMarco et al.

DiMarco et al teach the preparation of Polymorphic crystalline forms of epothilone analogues, pharmaceutical preparations containing the said analogues and method of treating cancer using the compostions. The epothilone analogues of DiMarco have the same structure as that claimed in the instant invention (col. 4). DiMarco suggests various dosages of epothilone analogues but not exactly the compositions containing separate vials of lyophilized compound and solvent and the specific carriers of the instant claims. However, the compositions in both sets

of claims contain essentially the same compound dissolved in suitable solvents. Accordingly, once present in solution both sets of compositions do not exhibit substantial differences unless shown otherwise. Accordingly it would have been obvious for a skilled artisan at the time of the instant invention to prepare a composition of epothilone analogue comprising a crystalline or a lyophilized form, wherein the compound is dissolved in the solvent or separated until use and still achieve the same pharmacological effect.

Claim Rejections - 35 USC § 103

Claims 15, 17-19, 22 and 56-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,380,395 to Vite et al (Vite) in view of US 4,950,432 to Mehta et al (Mehta).

Vite teaches epothilone derivatives for treating carcinomas, tumors, and a variety of human diseases (col. 5). The compounds of Vite read on the instant epothilone compounds (cols. 1-3). Vite teaches formulating the compounds for oral, intravenous and other routes of administration in the form of powders, solutions etc (col. 6). However, Vite does not teach the claimed lyophilization steps and reconstituting epothilone analog.

Mehta et al teaches macrolide antibiotics such as nystatin and amphotericin B and their encapsulation in to liposome for administration to the patient (col. 4). Mehta et al teaches that most of the macrolide antibiotics are limited by their hydrophobicity that precludes its systemic administration and therefore are administered only orally. Mehta et al teaches preparing liposome encapsulated macrolide antibiotics comprising the steps of dissolving phospholipids and antibiotics in solvents such as tell-butanol, methylene chloride, filtering and freezing the resultant mixture and finally lyophilization to produce a powder. It would have been obvious for

one of an ordinary skill in the art at the time invention to prepare epothilone derivatives encapsulated in liposome using the procedure of Mehta et al i.e., involving lyophilization steps to obtain a final powder and reconstitute the powders using desired solvents because Mehta et al teach macrolide antibiotics prepared by the above method are suitable for systemic administration and are stable for extended periods.

Claim Rejections - 35 USC § 112

Claim 58 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). These include: nature of the invention, breadth of the claims, state of the art, guidance of the specification, predictability if the art, and the working examples. All the factors have been considered with regard to the claim, with the most relevant factors discussed below.

All rejected claims are drawn to the methods of treating a patient with the administration of the instant composition. The nature of the invention is extremely complex because instant claims do not state what is being treated. The breadth of the claims exacerbates the complex nature of the claims. The claim encompasses treatment of a number of complex disorders that may have potential causes other than those disclosed in the specification. This may or may not be addressed by the administration of the composition. The composition may be administered to animals or mammals, thus encompassing a broad field of 'treatment". The state of the art

recognizes the administration of pharmaceutical compositions for treatment. The state of the art recognizes the treatment of the symptoms of these disorders.

Instant specification mentions a number of diseases or disorders however the specification fails to provide any guidance with respect to the administration of the instant composition makes practicing the claimed invention unpredictable. While the treatment of a number of diseases is known and taught in the art, instant claim is extremely broad and hence cannot be practiced without any guidance and thus becomes unpredictable as to what is being treated in a patient. Therefore, the practitioner would turn to trial and error experimentation to make/use the instant compositions for treating a patient, without guidance from the specification or the prior art. Therefore, undue experimentation becomes the burden of the practitioner.

Response to Arguments

Applicant's arguments filed 12-3-04 have been fully considered but they are not persuasive.

Double patenting Rejection: Applicants state that they need not address whether the argument that when the lyophilized material and/or crystalline material is placed in solution, the material dissolves such that the same compound is present, because instant claims are not directed to a solution of epothilone analogs, nor to a solution formed upon fully reconstituting lyophilized epothilone analogs and instead they are directed to a process for forming lyophilized epothilone analogs and their pharmaceutical preparations as well as methods of treatment. Applicants' arguments are not persuasive because instant claim recites reconstituting the

lyophilized product resulting in a solution and the patented claims also recite a solution formed from the crystalline polymorph of epothilone analog. Thus, both sets of claims result in a solution in which the morphology of the compound is no longer retained and thus have the same composition. Hence the rejection is maintained.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lakshmi S Channavajjala
Examiner
Art Unit 1615
February 5, 2005